REMARKS

Claims 1, 3, 5 and 7-16 are pending in the application. The claims have been amended to overcome indefiniteness rejections. No new matter has been added. Reconsideration is requested.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1, 3, 5 and 6-16 were rejected under 35 USC §112, second paragraph, as being indefinite. This rejection is traversed for the following reasons.

It was the Examiner's position that claims 1, 3 and 5 are indefinite because it is not clear whether the vaccine composition comprises a C-terminal fragment of SEQ ID NO:7 from *P. falciparum* 3D7 or comprises the C-terminal 42kD merozoite surface protein as set forth in SEQ ID NO:7. The claims have been amended to clarify that the vaccine composition comprises a C-terminal 42 kD fragment of merozoite surface protein-1 (MSP-1_{42}) from *P. falciparum* 3D7 as set forth in SEQ ID NO:7, i.e. that the vaccine comprises the protein of SEQ ID NO:7, and not a fragment thereof. Reconsideration and withdrawal of the rejection are requested.

Rejection Under 35 U.S.C. § 102(e)

Claims 1, 3 and 5 have been rejected under 35 USC § 102(e) as being anticipated by Hui et al. This rejection is traversed for the following reasons.

It is the Examiner's position that Hui discloses a vaccine composition comprising a sequence as set forth in SEQ ID NO:8 in an adjuvant, and that the disclosed protein is 100% identical to the claimed C-terminal fragment of the present invention. Applicants respectfully disagree. The claimed composition comprises a protein with the amino acid sequence set forth in SEQ ID NO:7 of the present application, having 391 amino acid residues. SEQ ID NO:8 of Hui contains only 375 amino acid residues. Thus, Hui does not contain each and every element of the invention as claimed in claims 1, 3 and 5.

Furthermore, it is respectfully submitted that the case made by Hui for native folding of baculovirus *P. falciparum* MSP-1_{42} (3D7), in example 16, is not convincing. He argues that

binding of recombinant antigen by mAb 5.2 is adequate for predicting correct structure and claims, without providing the evidence that reactivity of the *P. falciparum* MSP-1_{42} was dramatically lost when disulfide bridges were reduced. In fact, mAb 5.2 is not useful for characterizing structure because its respective epitope is not fully sensitive to disulfide bond reduction. As shown by Darko et al. (*Infect Immun* **73**, 287-297, 2005, enclosed for the Examiner's convenience), mAb 5.2 gives high levels of reactivity with reduced MSP-1_{42} in comparison with mAb 12.10, and 12.8 and other well known mAbs.

The present inventors have characterized the FMP1 protein against the same battery of disulfide dependent monoclonal antibodies shown in Darko et al (2005), with the same results. Most importantly mAbs 12.8 and 12.10, which have functional activity against *P. falciparum, in vitro*, and whose binding properties are highly dependant on structure, bind strongly to FMP1. Hui did not evaluate his antigen with these other mAbs.

Furthermore, the protein of Hui was produced using a baculovirus and silkworms, whereas the protein of the present invention was produced in *E. coli*. This results in differences in the properties of the proteins. It is well known from comparative vaccine trials, that N-glycosylation of MSP-1_{42} reduces functional antigenicity. Stowers et al. (*Proc Natl Acad Sci U S A* **99**, 339-344, 2002, enclosed for the Examiner's convenience) showed that a non-glycosylated form of MSP-1_{42} purified from transgenic mouse milk induced protective immunity in Aotus monkeys, while a glycosylated form did not. Similarly, Darko et. al (2005) showed that a non-glycosylated form of MSP-1_{42} expressed in *E. coli* induced a significant protective effect in Aotus monkeys, while a glycosylated form of MSP-1_{42} expressed in baculovirus did not.

These results also support Applicants' contention that the expression system is a limiting factor in the case of the present claims. The explanation for the different vaccine efficacies observed in these two studies is the presence of N-glycosylation. An expression system such as *E. coli*, which does not N-glycosylate protein, is superior to other expression systems, which do glycosylate protein.

For all of the above reasons, it is respectfully submitted that the presently claimed invention is neither disclosed nor suggested by Hui. Reconsideration and withdrawal of the

rejection are respectfully requested.

All objections and rejections having been addressed, it is respectfully requested that the rejections be withdrawn and a Notice of Allowance issued. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is hereby invited to telephone the undersigned at the number provided.

Respectfully submitted,

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